REMARKS

Entry of the foregoing, reconsideration of the restriction requirement and examination of all of the claims on the merits are respectfully requested in light of the following remarks:

STATUS OF CLAIMS

Claims 1-35 and 56-98 remain in this application. Claims 36-55 were previously cancelled.

Claim 6 has been amended hereinabove to correct an obvious clerical error.

Claim 67 has been amended above to specify that the claimed process is for the preparation of a complex cladribine-cyclodextrin complex as claimed in Claim 56. This limits the process of Group III, Claim 67 (and its dependent claims) to the preparation of a complex of Group I, Claim 56.

RESTRICTION REQUIREMENT

The Examiner has required election of a single invention, which he considers is one of Group I, Claims 1-12, 56-66 and 82-98, drawn to the cladribine-cyclodextrin complex and pharmaceutical compositions thereof; Group II, Claims 13-35, drawn to methods of enhancing the oral bioavailability of cladribine or treating symptoms of a cladribine-responsive condition; and Group III, Claims 67-81, drawn to a process of making. Applicants hereby elect, with traverse, Group I, Claims 1-12, 56-66 and 82-98.

The requirement is traversed because the claims are indeed so linked as to form a single general inventive concept under PCT RUle 13.1. The claims in Groups I-III all have the same special technical features and those are, in fact, the features of the claimed complex. This is not simply any cladribine-cyclodextrin complex, as the Examiner seems to think, however, but rather, a very specific complex which is a complex cladribine-cyclodextrin complex which is an intimate amorphous admixture of (a) an amorphous inclusion complex of cladribine with an amorphous cyclodextrin and (b) amorphous free cladribine associated with amorphous cyclodextrin as a non-inclusion complex (Claim 56). The claimed composition comprising this complex is a pharmaceutical composition comprising a complex cladribine-cyclodextrin complex which is an intimate amorphous admixture of (a) an amprphous inclusion complex of cladribine with an amorphous cyclodextrin and (b) amorphous free cladribine associated with amorphous cyclodextrin as a non-inclusion complex, formulated into a solid oral dosage form (Claim 1).

The Examiner has ignored the amorphous nature of the entities which constitute the claimed complex cladribine-cyclodextrin complex and the solid oral dosage forms containing it, which amorphous entities maximize or enhance the benefits of complexation in terms of bioavailability and interpatient variation when administered in solid oral dosage form. Thus, the Examiner has ignored the novel and inventive features of the claimed complex in assessing the claimed subject matter.

Schultz et al. U.S. Patent No. 6,194,395, does not disclose a solid oral dosage form of a complex as claimed in present Claim 1, or the instantly claimed complex itself, either explicitly or inherently. The Examiner refers to the formation of

an inclusion complex with cyclodextrin to be a reversible process governed by an equilibrium and therefore inherently comprises both an inclusion complex and a non-inclusion complex. The process which the Examiner refers to can occur only in solution. Applicants' claims are limited to a complex cladribine-cyclodextrin complex which is an amorphous admixture of (a) an amorphous inclusion complex and (b) amorphous free cladribine associated with amorphous cyclodextrin as a non-inclusion complex, and to solid oral dosage forms containing these. The word "amorphous" is defined on page 9 of the specification as referring to a noncrystalline solid. Schultz et al. do not describe any actual work done with solid oral dosage forms. In fact, they describe only one general method of preparing a solid dosage form, which is a melt extrusion process, in which the cladribine and cyclodextrin are mixed with other optional additives and then heated until melting occurs. The Schultz et al. patent does not describe or suggest a method for enhancing or maximizing the bioavailability of cladribine from a solid oral dosage form or a complex or composition specially designed to do so. The reference is moreover silent about amorphous forms; and applicants' amorphous inclusion complex and other amorphous materials are in no way inherent in what Schultz et al. describe.

Schultz et al. U.S.P. 6,194,395 was correctly classified as a general state-of-the-art "A" reference in the International Search Report, a copy of which was provided with applicants' First Information Disclosure Statement of November 14, 2006. Applicants are submitting with the accompanying Fourth Information Disclosure Statement a copy of the International Preliminary Report on Patentability issued in connection with the international phase of this application. In particular, we draw the Examiner's attention to the Written Opinion of the International Searching

Authority (ISA) issued by the European Patent Office in its capacity as ISA, in particular the remarks regarding novelty, inventive step and industrial applicability. The present Examiner's position, which is contrary to a reasonable interpretation of the art as pointed out above, is also contrary to the opinion of the International Searching Authority.

For the reasons set forth above, it is respectfully submitted that the restriction requirement is without merit as the Examiner's basis for it is not sound. Withdrawal of the restriction requirement and examination of all of the claims on the merits are respectfully requested.

Respectfully submitted,

BUCHANAN INGERSOLL & ROONEY PC

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By: Mary Katherine Baumeister
Mary Katherine Baumeister
Registration No. 26254

P.O. Box 1404
Alexandria, VA 22313-1404
703 836 6620